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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,691	06/03/2002	Stephen Gill	PA-9947	3741

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EXAMINER	
JONES, DAMERON LEVEST	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/069,691	GILL ET AL.	
	Examiner	Art Unit	
	D L. Jones	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 2/2/10 wherein claim 1 was amended.

Note: Claims 1-14 are pending.

APPLICANT'S INVENTION

2. Applicant's invention is directed to composition which comprises a radiopharmaceutical in a container which has a silica coating on the inner surface, the improvement being that the radiopharmaceutical comprises a coordination complex of Formula MLn wherein M is the radiometal of the radiopharmaceutical and L is a organic ligand which is a carbon containing compound which comprises 2, 3, 4, 5, 6, or 8 heteroatoms selected from N, O, S, P, or Se. The variable n is the number of ligands (L) attached to M and is an integer of value 1 to 8.

RESPONSE TO APPLICANT'S AMENDMENTS/ARGUMENTS

3. The Applicant's arguments and/or amendment filed 2/2/10 to the rejection of claims 1-14 made by the Examiner under 35 USC 103 and/or 112 have been fully considered and deemed persuasive-in-part for the reasons set forth below.

103 Rejection

The 103 rejection is WITHDRAWN because Applicant has amended the claims to overcome the rejection. In particular, the claims have been amended to require 2-6 or 8 heteroatoms present in the chelating agent.

New Matter Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims contain new matter because review of the does not set forth wherein Applicant's variable L was referred to as 'a non-radioactive organic ligand'. Instead, throughout the specification, the variable L is referred to as the 'organic ligand'. Thus, the phrase '***non-radioactive*** organic ligand' contains new matter. While the phrase, 'non-radioactive organic ligand' appears in independent claim 1, line 7, claims 2-14 depend on independent claim 1. As a result, those dependent claims (claims 2-14) also contain new matter.

APPLICANT'S RESPONSE

Applicant asserts that since claim 1 has been amended to reinstate the previous acceptable claim language ('organic ligand'), the rejection is overcome.

EXAMINER'S RESPONSE

While Applicant has amended independent claim 1 to contain the language 'organic ligand', the phrase '***non-radioactive*** organic ligand' is found in claims 6 and 8. In addition, it is noted that claims 7 and 9 depend on claim 6; thus, claims 7 and 9 are also rejected as containing new matter.

NEW GROUNDS REJECTIONS

103 Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rajopadhye et al (US Patent No. 5,888,970) in view of Yamaguchi et al (JP 11-99192)

in further view of Schott Glaswerke (DE 29,609,958) or Walther et al (US Patent No. 6,200,658).

Once again, it is noted that Board of Patent Appeals and Interferences decision on 8/27/09 concluded that secondary references (Yamaguchi et al, Schott Glaswerke, and Walther et al) establish that a radiopharmaceutical in a container which has a silica coating on the inner surface is obvious in the art (for a detailed explanation of the secondary references and the Board of Patent Appeals and Interferences decision, Applicant is respectfully requested to review the office action mailed 8/27/09). Thus, in an attempt to overcome the prior art, the claims have been amended to the limitation that L is a carbon-containing chelating agent which comprises 2-6 or 8 heteroatoms selected from N, O, S, P, or Se.

Rajopadhye et al disclose labeled chelators that are incorporated into cyclic peptides that are useful as imaging agents (see entire document, especially, abstract; column 15, lines 9-24). In particular, the chelators may contain 2-10 heteroatoms selected from N, S, and O (column 3, lines 1-23). Possible chelators having various combinations of nitrogen, sulfur, and oxygen heteroatoms are disclosed in column 10 (lines 1-65), column 11 (lines 1-45), column 12 (lines 10-65), column 13 (lines 1-65), column 14 (lines 1-15); column 25 (lines 26-45), column 27 (lines 6-24), and column 28 (lines 16-60). The complexes may include radionuclides such as 99mTc and 111In (column 11, lines 55-59; columns 14-15, bridging paragraph). In addition, Rajopadhye et al disclose kits that may include the radiopharmaceuticals. The kits may contain one or more vials and all or part of the formulation may independently be in the form of a

sterile solution or a lyophilized solid (column 16, lines 12-44). The kit may also contain solubilization aids such as butyl paraben (column 16, lines 52-59; column 30, lines 22-26). In addition, the kits may comprise a bacteriostat to inhibit the growth of bacteria in the kit during storage or before or after the kit is used to synthesize the radiopharmaceutical. Thus, while Rajopadhye et al disclose a radiopharmaceutical comprising a complex with an organic ligand which is carbon-containing chelating agent comprising 2, 3, 4, 5, 6, and 8 heteroatoms selected from N, O, and S, a metal, and a kit which may comprise one or more vials and a bacteriostat, the reference fails to disclose that the container (e.g., vial) is silica coating on the inner surface. In addition, the reference fails to state that possible heteroatoms useful with their chelators include P and Se.

Yamaguchi et al disclose containers for radiopharmaceuticals and radiopharmaceutical preparations using the container. The objective of Yamaguchi et al was to develop containers for pharmaceutics which can prevent highly adsorbable radiopharmaceuticals from being adsorbed thereon and provide a clear description of their contents and the amounts thereof (see entire document, especially, page 1; page 3, 'Detailed Description of the Invention'; page 6, paragraph [0008]; page 7, paragraph [0011]). Yamaguchi et al solved the problem by coating the interior surface of a glass container with silica that is used to house radiopharmaceuticals (page 2, entire page; and page 3, claim 4). In claim 5, Yamaguchi et al invention is directed to a radiopharmaceutical preparation which is characterized in that a radiopharmaceutical container (the container is glass) has an interior surface that is coated with silica and

filled with an adsorbable radioactive material (page 3, claim 5). Also, it is disclosed in the prior art, radioactive materials are used as tracers for diagnostic imaging in medical fields and that in some instances, a single element is used as the radioactive material and in other instances, label compounds are used which have specific in vivo behavior (page 4, paragraph [0002]. In addition, it is disclosed that detailed method of coating the interior surface of a glass container with silica are known in the art and are commercially available under the name of Silicoat (the containers are made by Fuji Glass Corp.) (pages 7-8, bridging paragraph). It should be noted that while Yamaguchi et al discloses the use of thallium chloride as the radioactive material, the reference teachings are not limited to thallium chloride.

Walther et al disclose numerous applications for hollow glass bodies made from low melting glass material which requires an increase in the chemical resistance of the interior surface of the glass body. In order to avoid a disadvantageous dealkalizing process, the interior surface of the hollow glass body is coated. The interior surface may be coated with SiO2 (silicon dioxide, commonly known as silica) having a predetermined coating thickness according to the required chemical resistance or working conditions for forming the glass body. The coating is advantageously provided by means of a plasma chemical vapor deposition (PCVD) process (see entire document, especially, abstract; column 4, lines 39-44; and columns 4-5, bridging paragraph)

Schott Glaswerke discloses glass containers useful for storing pharmaceuticals and diagnostic solutions (see entire document, especially, page 1, first paragraph). One

of the objects of Schott Glaswerke was to find a glass container for storing pharmaceutical or diagnostic solutions that remain largely inert with respect to the solutions (e.g., it was the desire of Schott Glaswerke to minimize the quantities of ions that leach out of the glass when storing the pharmaceutical or diagnostic solutions) (page 2, second complete paragraph). The problem of leaching of ions out of the glass was solved by coating the interior surface of the glass container with a layer of SiO2 (page 2, fourth complete paragraph; page 3, first paragraph). The layer may be generated by means of plasma chemical vapor deposition (PCVD) (page 2, fourth, fifth, and sixth complete paragraphs). In addition, Schott Glaswerke disclose that the composition of the glass of which the container is made is not critical, so long as the interior is coated with SiO2 (page 3, second, third, and fifth paragraphs; and page 4, 'Comparison' table and first paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Rajopadhye et al using the teachings of Yamaguchi et al, Schott Glaswerke, and Walther et al to coat the inner surface of a container that has a radiopharmaceutical (the radiopharmaceutical comprises a coordination complex of a metal and an organic ligand) with silica for the reasons below. (1) Yamaguchi et al, Schott Glaswerke, and Walther et al all disclose various advantages of using glass vials that are coated with silica. (2) Both Yamaguchi et al and Schott Glaswerke disclose advantages of using glass with silica coated interiors for radiopharmaceuticals. (3) A skilled artisan would have been motivated to use a silica coated glass interior in the invention of Rajopadhye et al in order to take advantage of

one or all the advantages known in the art to be associated with silica coated interiors (i.e., avoid leaching of ions, provide a clear description of the container contents and the amounts thereof, etc.). (4) Also, skilled artisan in the art would be motivated to use PCVD to coat the interior surface with silica because Schott Glaswerke and Walther et al disclose that it is well known in the art to use plasma chemical vapor deposition for coating glass surfaces with silica and the advantages of the process. In particular, Schott Glaswerke and Walther et al disclose that glass containers coated with PCVD are significantly more resistant to leaching. (4) Furthermore, it would also be obvious to generate a kit comprising the radiopharmaceutical metal complex wherein the metal complexes may include P and Se because a skilled artisan would not only recognize that all the heteroatoms (N, O, S, P, and Se) of interest in the instant invention are non-metals from Groups VA and VIA, but would recognize that the replacement of one equivalent with another from the same Group would not drastically alter the overall properties of the contrast agent.

Since Rajopadhye et al, Yamaguchi et al, and Schott Glaswerke are all directed to radiopharmaceuticals, the references may be considered to be within the same field of endeavor. Thus, the reference teachings are combinable. Furthermore, since, Schott Glaswerke, Yamaguchi et al, and Walther et al all are directed to silica coated glass interiors, the references may be considered to be within the same field of endeavor. Hence, those reference teachings are combinable.

COMMENTS/NOTES

4. It should be noted that Yamaguchi et al (JP 11-99192) and Schott Glaswerke (DE 29,609,958) were previously mailed to Applicant.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D L. Jones whose telephone number is (571)272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m.. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor,

Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/D L. Jones/
Primary Examiner
Art Unit 1618

May 17, 2010